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Distribution of Genotypes at Codon 171 in U.S. Sheep

If exposed to scrapie, sheep with specific genetic variations at codon 171 have been found to be either susceptible or more resistant to developing clinical signs of scrapie. Scrapie can present as a chronic, progressive, neurologic disorder and is eventually fatal. However, many cases remain undiagnosed because the clinical signs are subtle or the sheep are culled before clinical signs appear. It is thought to be caused by an infectious protein or prion, and has a very long incubation period. There is currently only one live animal test for scrapie. It requires biopsy of the lymphoid tissue of the third eyelid, the tonsil, or a lymph node. Prions are resistant to most disinfectants and can be transmitted by sheep that do not display clinical signs of the disease. Therefore, to reduce the risk of scrapie, sheep producers should purchase new animals from known scrapie-free flocks, and focus on management practices such as flock certification, genetic testing for resistance, and hygienic lambing management.

The USDA's National Animal Health Monitoring System (NAHMS) collected data on sheep health and management practices from a stratified random sample of sheep production sites in 22 States¹ as part of the Sheep 2001 study. These States represented 87.4 percent of the U.S. sheep inventory and 72.3 percent of U.S. sheep producers. Health-related management practice information was collected from 3,210 participating operations in the first interview from December 29, 2000, to January 26, 2001. Of the original participants, 1,101 were interviewed a second time between February 5 and April 27, 2001. Of these operations, 687 (62.4 percent) volunteered to have blood samples collected from their sheep for genotyping at codon 171; 11,748 samples were tested for genotyping from these operations.

¹ Arkansas, California, Colorado, Idaho, Illinois, Indiana, Iowa, Kansas, Montana, Minnesota, Nevada, New Mexico, Ohio, Oregon, Pennsylvania, South Dakota, Texas, Utah, Virginia, Washington, Wisconsin, Wyoming

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Genotyping

Genotyping is **not a test for scrapie**, but rather a test looking for certain information encoded on the PrP gene. This encoded information helps determine the susceptibility of sampled sheep to developing clinical disease from scrapie should the animal be exposed.

Genotyping was offered to participating producers to examine the distribution of genotypes in the U.S. sheep population. DNA from each submitted blood sample was extracted from the nuclei of white blood cells normally found in an animal's blood. The DNA samples were then sent to a genotyping facility to determine the scrapie-related PrP gene codon 171 genotypes.

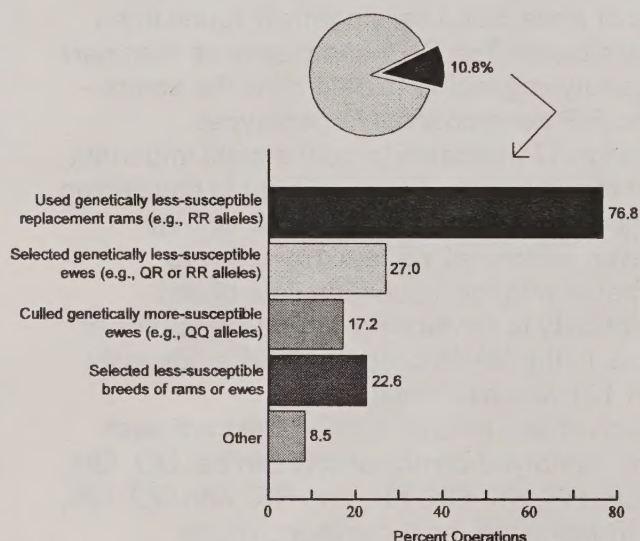
Codon 171 appears to be the most important codon for determining susceptibility to developing clinical disease from scrapie in U.S. sheep. However, codons at 136 and 154 also are associated with the incubation time of and susceptibility to developing clinical symptoms of scrapie. In the NAHMS Sheep 2001 study, only codon 171 was examined.

Each sheep inherits a PrP gene from each parent. Genotype combinations can be: QQ, QH, HH, QR, HR, KK, QK, KR, and RR, with QQ, QR, and RR being the most common. These combinations are an indication of the animal's likelihood of developing clinical signs of scrapie if exposed to the scrapie agent. QQ sheep are the most likely to become clinically ill when exposed to scrapie; RR sheep are the least likely to develop clinical disease. The H alleles are rare. They appear to behave similarly to Q alleles but more research needs to be done to better understand the role of the H allele in this disease. The K allele is very rare and its effect on scrapie susceptibility has not been studied.

Current Management Practices Related to Genotyping at Codon 171

With careful record keeping and strict breeding practices, genotyping can be a useful tool in the prevention and control of scrapie. Of the 92.6 percent of operations that had at the very least heard of scrapie, 10.8 percent reported using genetic selection to control or prevent the disease. Of those operations, three-fourths (76.8 percent) selected replacement rams that were genetically less susceptible to scrapie (e.g., RR alleles), and about one-fourth (27.0 percent) selected genetically less susceptible ewes (Figure 1). Most of the operations that reported the method of genetic selection as "other" (8.5 percent) indicated they kept a closed flock or did third eyelid testing for scrapie.

Figure 1. Percent of Operations (10.8 percent) That did any Genetic Selection for Scrapie Control, and of Those, Percent of Operations That Carried Out the Following Practices



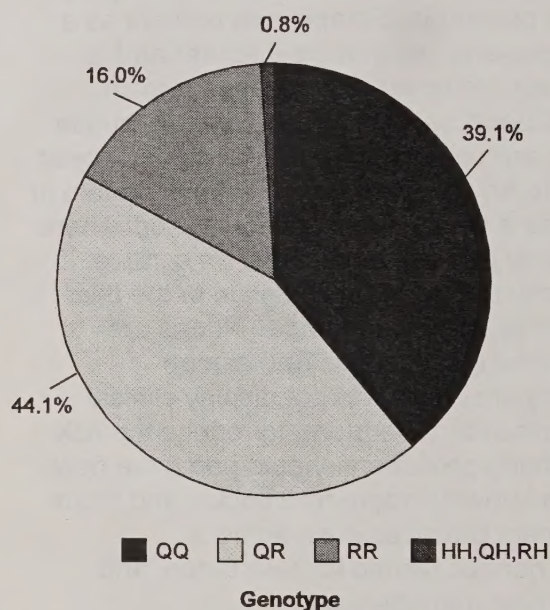
Results of NAHMS Testing

The following results may not be representative of all sheep in the sample population. Overall, 11,748 blood samples were genotyped. Samples were collected from animals representing the following breeds: Border Leicester, Cheviot, Clun Forest, Columbia, Corriedale, Dorset, Finnsheep, Hairsheep, Hampshire, Jacob, Karakul, Lincoln, Merino, Montadale, Navajo Churro, Oxford, Polypay, Rambouillet, Romney, Romanov, Scottish Blackface, Shropshire, Southdown, Suffolk, Targhee, Texel, and crosses. The most common breeds were Suffolk (24.1 percent), Rambouillet

(17.0 percent), Dorset (8.7 percent), Columbia (7.1 percent), and Targhee (5.5 percent).

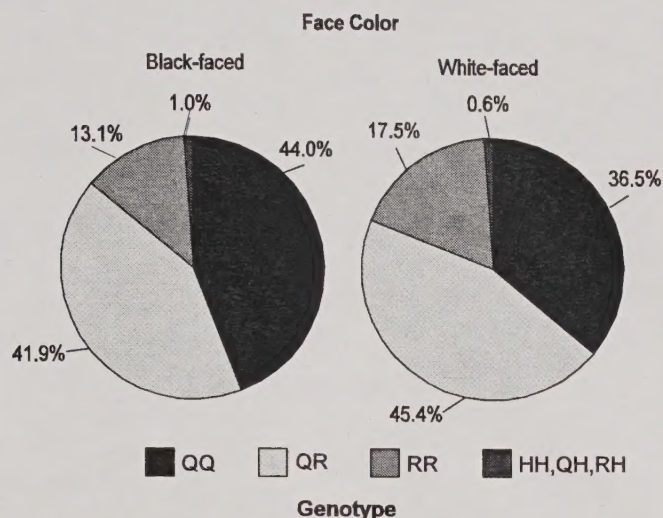
The distribution of genotypes for all sheep was: 39.1 percent QQ; 44.1 percent QR; 16.0 percent RR; and 0.8 percent H allele variations (QH, RH, HH) as shown in Figure 2 (no test was conducted for the K allele). Although for some breeds very few animals were tested (e.g., seven Scottish Blackface sheep), all breeds tested had at least one animal with an R allele.

Figure 2. Percent of All Sheep by Genotype



There was a difference in distribution of genotypes between black-faced breeds and white-faced breeds (Figure 3). Because face color was not requested on the testing form, it was assumed the actual face color of the animal tested was typical of the reported breed. Black-faced breeds included: Hampshire, Oxford, Southdown, Suffolk, Navajo Churro, Romanov, Karakul, Clun Forest, Scottish Blackface, and black-faced crosses. White-faced breeds were all others that could be defined, apart from hairsheep. Black-faced breeds had a higher percentage of QQ animals (44.0 percent) than white-faced breeds (36.5 percent). Non-British origin black-faced breeds (Karakuls, Romanov, Navajo Churro) had a high percentage of RR genotype animals (25.3 percent) compared to all other black-faced breeds (12.7 percent).

Figure 3. Percent of Sheep by Face Color and by Genotype



The most economically efficient way for the genotype of a flock to change from animals with predominantly Q alleles to those with predominantly R alleles is to breed with an RR ram. Although Sheep 2001 showed that the percentage of rams homozygous for the R allele was higher than the percentage in ewes (17.3 percent versus 15.8 percent), the difference was not significant.

Conclusion

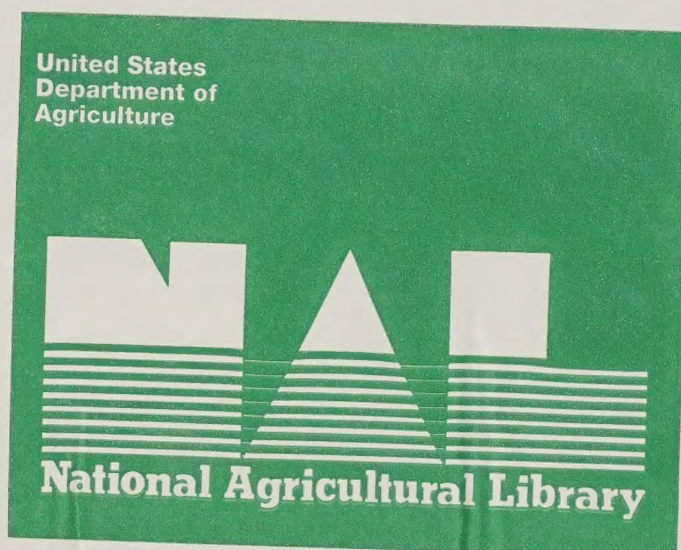
Adjusting genotypes in a flock is only one tool to control scrapie. Good biosecurity, knowledge about the flock history of new additions, flock certification, and hygienic lambing management are all important management tools for scrapie control and prevention.

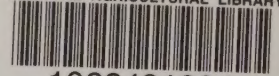
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